Determination of a brief AUDIT screening questionnaire to identify women at risk of harmful and hazardous alcohol consumption in primary care settings

By

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DECLARATION

I, *VASILIKI VICKY GRACE LABADARIOS* hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Part A: The protocol

Abstract

Alcohol consumption in South Africa is a major driver of the quadruple burden of disease[1], with an estimated cost to society of 10-12% of GDP in 2009. Additionally, South Africa has the highest rates of Foetal Alcohol Syndrome in the world. As effective interventions are available for hazardous and harmful drinking, screening for this behaviour in primary care can potentially contribute to improving health outcomes and reducing the cost to society.

Existing validated screening questionnaires are available to identify those who drink alcohol at hazardous or harmful levels. However, no questionnaires have been validated for women of childbearing age in South Africa. The purpose of this study is to determine such a questionnaire, with sensitivity and specificity balanced for South African primary care settings.

The accuracy of existing brief screening questionnaires will be tested against the full AUDIT questionnaire as the gold standard. The most accurate brief screening questionnaire will assist in the rapid, accurate identification of women of childbearing age attending primary care facilities who will benefit from brief interventions to reduce their alcohol intake, thereby improving their own health and reducing the risk of future alcohol exposed pregnancy. [208 words]

[1] Quadruple burden of disease – HIV/AIDS and TB, Maternal and child mortality, Non-communicable diseases and violence and accidents

Background:

Harmful and hazardous alcohol consumption in South Africa is a major public health concern (Jacobs & Steyn, 2013) which contributes both directly and indirectly to the well-documented quadruple burden of disease (Matzopoulos, et al., 2014). Alcohol intoxication is associated with interpersonal violence and accidents, resulting in morbidity and mortality (Seedat, et al., 2009). Individuals with harmful and hazardous drinking habits are at greater risk of poor self-management of concurrent illnesses, such as HIV and AIDS, and therefore as a group experience poorer outcomes, including an increased risk of death (Morojele, et al., 2016). Sustained, excessive alcohol consumption increases the risk of developing non-communicable diseases, such as diabetes, cardiovascular disease and certain types of cancers (Rehm, et al., 2010). Affected individuals who continue to drink to excess are less likely to be diligent in the self-care required for the successful management of their condition, leading to increased complication rates and increased likelihood of premature death (Bhana, et al., 2017). Sustained excessive, alcohol consumption is causally related to the development of mental illness and exacerbates existing mental illness over and above the addiction and abuse related to alcohol itself (Saban, et al., 2014).

Agricultural regions of the Western Cape Province of South Africa report the highest rate of Foetal Alcohol Syndrome in the world (May, et al., 2007) (Olivier, et al., 2013) (May, et al., 2016). Intoxication is associated with risky sexual behaviour, which can result in unplanned and perhaps unwanted pregnancies associated with increased financial, psychological and physical stress. Additionally, the risk of contracting sexually transmitted infections is increased, which can affect both mother and child (Burnhams, et al., 2014) (Bello, et al., 2017).

Alcohol can therefore be said to have a multi-level impact on the quadruple burden of disease - as a necessary cause for diseases caused only by alcohol such as alcohol use disorders or alcohol related birth defects, a contributory cause for the genesis of diseases such as non-communicable diseases and as

an exacerbating factor for many of these diseases resulting in less favourable outcomes.

Addressing this single factor has the potential to impact significantly on health outcomes and life expectancy related to these national priority conditions. However, the identification of individuals at risk can be difficult due to several factors. Firstly, social desirability bias may influence patients to under-report their alcohol intake when questioned (Muggli, et al., 2015). Secondly, the implementation of existing screening questionnaires (Alcohol Use Disorders Identification Test - AUDIT) which have been shown to be effective in the identification of at-risk drinkers are considered too time consuming to implement in South Africa's over-utilised and understaffed primary care services (Mash, et al., 2015) (Rispel, 2016), which are the ideal settings for identification of individuals who may benefit from intervention.

In 1980, a WHO expert committee recommended the development of efficient methods for identification of individuals with hazardous or harmful levels of alcohol consumption, prior to the development of related health and social consequences. The AUDIT questionnaire was developed by the WHO Collaborative Project on Identification and Treatment of Persons with Harmful Alcohol Consumption in response to this recommendation (World Health Organisation, 2018).

The questionnaire is designed to be applicable across cultures and genders (Babor & Grant, 1989) (Saunders, et al., 1993). Questions 1-3 relate to alcohol consumption, questions 4-6 measure alcohol dependence symptoms and questions 7-10 determine alcohol-related problems. The questions for the AUDIT screening test are asked with reference to the preceding 12 months. The response to each question is measured by a five point Likert scale. Responses are summed for an overall score ranging from 0-40. Scores are then categorised into low risk (0-7), alcohol use in excess of low-risk guidelines (8-15), hazardous or harmful drinking (16-19; likely to result in harm eventually) and high-risk (20 or more; definite harm with the likelihood of current alcohol dependence) (World Health Organization, 2001).

Abbreviated versions of the AUDIT questionnaire have been identified to facilitate utilisation in busy, high pressure clinical care settings (Reinert & Allen, 2007). However, it is not clear whether the abbreviated questionnaires will be as accurate in South African health care settings, as binge drinking is particularly prevalent in South Africa and existing screening questionnaires may not accurately identify individuals at risk as a result of this drinking pattern (Peltzer, et al., 2011).

An article evaluating AUDIT questionnaire performance has suggested that, as women are at risk of harm from alcohol in different ways to men, it may be of benefit to identify a specific subset of AUDIT questions applicable specifically to women (Reinert & Allen, 2007).

Optimal brief AUDIT screening questionnaires for utilisation in HIV clinics in South Africa have been identified (Morojele, et al., 2016). This study reported differing performance of the various screening questionnaires by gender. However, no similar analysis has been conducted to identify optimal screening questionnaires specifically for women of childbearing age attending primary care facilities.

A study in the US identified a screening questionnaire consisting of a single question from the Quick Drinking Screen, ("During the previous three months, how often did you have four or more drinks on one occasion?") which successfully identified women at risk of hazardous and harmful drinking due to binge-drinking (>85% for current drinkers) (Stewart, et al., 2010). This study was replicated in Russia with similar results (99% success) (Balachova, et al., 2015). However, a previous study in South Africa repeated the analysis using AUDIT 3 ("How often do you have six or more drinks on one occasion?"), which showed that this single question screening questionnaire was not suitable for the South African population (Morojele, et al., 2016).

The CAGE questionnaire, developed in 1970 and validated for use in primary care to identify problem drinking (Mayfield & Hall, 1974) (Fiellin, et al., 2000), has been used previously in South African studies (London, et al., 1988) (Peltzer, et al., 2011) (McLoughlin, et al., 2013) (Rendall-Mkosi, et al., 2013)

(Gossage, et al., 2014) (Morojele, et al., 2016). It consists of four questions – has the individual felt the need to **C**ut down on their drinking, have they ever been **A**nnoyed for being criticised for drinking, have they ever felt **G**uilty about their drinking and have they ever needed an **E**ye opener to get rid of a hangover first thing in the morning. A positive answer for two or more of the questions indicates the likelihood of problem drinking (Mayfield & Hall, 1974).

Brief Motivational Interviewing has been shown to be effective in achieving sustained reductions in alcohol intake (De Vries, et al., 2015) (Montag, 2016).

Although primary care is the ideal setting for the implementation of a national screening programme to identify individuals at risk of hazardous and harmful drinking (Fiellin, et al., 2000) (World Health Organisation, 2018), the primary care setting in South Africa is currently overstretched due to inadequate numbers of available health care professionals and large numbers of patients requiring care (Rispel, 2016). For such a programme to be successful, it is therefore essential that the proposed screening requires minimal time for administration, is easy to apply and has high sensitivity and specificity to avoid time wasted in full evaluation of individuals with false positive screening results.

This study seeks to identify such a questionnaire for use in women aged 18-44 years. The study focusses on women as drinking patterns are frequently gender based, as are the physical consequences of alcohol consumption (Reinert & Allen, 2007) (Erol & Karpyak, 2015). The focus on women in their reproductive years is justified in view of the particular burden of Foetal Alcohol Syndrome in South Africa. Furthermore screening criteria for adolescents and older adults may be different to those for adults (Reinert & Allen, 2007).

Aim:

To determine a brief screening questionnaire for the identification of harmful and hazardous drinking in women of reproductive age.

Objectives:

1. To compare the accuracy of different subsets of AUDIT and CAGE questions in identifying women at risk of hazardous and harmful drinking, in relation to the full AUDIT questionnaire as the gold standard.
2. To determine whether residence location (urban/rural) affects the sensitivity and specificity of the different screening questionnaires
3. To determine whether binge drinking (defined as five or more drinks on one occasion for women) affects accuracy of the screening questionnaires in identifying the risk of hazardous and harmful drinking.
4. To determine whether a single question can be used to identify individuals with a high likelihood of dependent drinking.

Purpose:

1. Enable swift, accurate identification of women at risk of harmful and hazardous drinking in primary care settings for referral to alcohol management programmes, which in turn will contribute to
    a. Reducing the risk of developing alcohol related health problems in women
    b. Reducing the risk of alcohol exposed pregnancy (AEP) in women in their reproductive years
2. Formulate recommendations for national policy and guidelines on screening in primary care settings for hazardous and harmful alcohol consumption in women of reproductive age

Methods

An existing dataset will be utilised for this study, which was collected in rural and urban areas of South Africa in 2006. Ethics approval was granted by the Health Sciences Research Ethics Committees of the University of Pretoria (UP HREC Ref# 121/2005) and University of Cape Town (UCT HREC Ref# 381/2005).

This data set was collected for a study describing alcohol use patterns amongst women aged 18-44 in urban and rural areas, with the intention of understanding factors influencing risky drinking, which in turn put the women at risk of AEP. Those at risk of AEP are also at risk of the health consequences of hazardous and harmful drinking. It is therefore proposed to utilise this dataset to identify a subset of the AUDIT and/or CAGE questions to identify women at risk of harmful and hazardous alcohol consumption.

The parent study was an observational cross-sectional study.

Data was collected from two sites – one urban and one rural – based on evidence in the literature regarding high risk populations and the experience of the researchers. The urban study site was in the City of Tshwane in Gauteng Province and included Mamelodi, the Moot and Eersterust, with a combined population of around 340 000 at the time of the survey. Tshwane Municipality, which includes Pretoria and its surrounding areas, is a typical South African metropolitan area with long established townships and suburbs. Since the 1990's, there has been increasing racial integration in middle class areas, but the old township areas remain inhabited principally by a single race group. Mamelodi was established in 1953, 20km east of Pretoria (Gauteng Tourism Authority, 2018). It is a densely populated township which is home to mainly working class people of African descent. Eersterust has a population of mainly 'coloured[1]' Afrikaans-speaking people (Eersterust - Our Community, 2018). The main African languages spoken are sePedi and seTswana, with many other languages represented in the population. Most suburbs in the Moot, situated north east of the city centre, were established in the early 1900's. It is

home to the Union Buildings and Steve Biko Academic Hospital. The population is mainly white[2], with English and Afrikaans being the predominant spoken languages.

The rural site was selected in the Western Cape and included Cederberg, Bergrivier, and Swartland municipalities, representing a population of just under 160 000 at the time of the survey. The majority of the working class people living and working on the farms in these areas are Afrikaans speaking 'coloured[1]' people. In both provinces, data was collected by means of a household survey administered by trained interviewers.

Data were collected in relation to eight categories:

1. Demographics
2. Level of connectedness / social support structures
3. Health perceptions
4. Use of reproductive health services
5. Pregnancy experiences and fertility norms
6. Drinking and smoking patterns
7. Cultural beliefs and practices related to substance use, in particular during pregnancy
8. Knowledge of alcohol and pregnancy / child development

As part of the data collection process, AUDIT and CAGE questionnaires were administered to all women who did not abstain from alcohol.

[2] Under apartheid, people from different ethnic backgrounds were classified as "white", "indian", "black" (African) or "coloured" (mixed race). These terms were markers of social stratification under apartheid and the social context of these groups may be associated with other patterns of alcohol use and dependence. Use of these terms is made here to recognise these social markers and not to signify a genetic difference.

Sampling

Sample size

Sample size was calculated based on a power of 0.85, an estimated prevalence of 10% for risky drinking, completed primary education amongst risky drinkers of 40% and amongst non-risky drinkers of 58% (known example of a risk factor utilised for the power calculation), and a significance level of 0.1. This resulted in an estimated sample size of 750 in the urban area and 619 in the rural area. To ensure an adequate number of participants to achieve the required power, the sample size was adjusted upwards using the variance inflation factor (VIF) given by (1/1-ρ2) on the computed sample, where ρ2 is the squared multiple correlation of the covariate of interest to 790 for the urban population and 650 for the rural population.

The study population was the total population of women aged 18-44 years within the geographical areas defined above, representing a total population of around 500 000.

Different sampling methods were employed in each site. For the urban site, cluster random sampling was applied. Eighty-two census enumeration areas were selected, from which ten households were randomly selected, identified with the assistance of aerial photographs. One woman aged 18-44 years was randomly selected from each household and invited to participate in the survey.

For the rural site, stratified cluster random sampling was applied. For the first stratum, farms were selected within the relevant municipalities, proportional to the total number of farms in each municipality. Using this proportional approach, at total of 150 farms were randomly selected from a total population of 1450 farms in the three municipalities. This number represented oversampling, to allow for uncontactable, ineligible and non-functional farms. For the second stratum, within each farm all women aged 18-44 years in every household were invited to participate in the survey. This sampling method was chosen as there are on average only seven households per farm and the farms are separated by large geographical distances.

In rural and urban settings, a trained fieldworker visited each selected household and interviewed the female householders aged 18-44 years , as per the sampling strategy. No incentives to participation were offered.

Inclusion / exclusion criteria

Only females aged between 18 and 44 years were eligible for inclusion.

Pregnant and non-pregnant women were included, as the aim of the study is to identify appropriate screening to be implemented in advance of conception.

Women who had never consumed alcohol or were not current drinkers were excluded from this analysis as their experiences would not provide additional information relating to the performance of the screening questionnaires.

Women who declined to participate were excluded.

Validity

Using the total population of the geographical area of interest as the sampling frame for random selection rather than a self-selected proportion of the population, such as those attending a health establishment, will result in data more accurately reflective of the true population parameters and therefore more generalisable to other populations within South Africa.

Using an interviewer to collect the data rather than requesting participants to complete forms may assist participants to understand the information required more fully, resulting in more accurate responses.

Visiting participants in their own homes may provide reassurance regarding the confidentiality of the information collected as well as provide reassurance that information in relation to alcohol consumption in particular will not have any perceived negative consequences, such as referral to social services if their consumption is considered harmful. For these reasons, subjects may be less likely to under-report alcohol consumption.

Reliability

Interviewers were trained in administration of the questionnaire, which consisted of closed ended questions.

Fieldworkers

Twelve female fieldworkers were recruited from communities local to the survey, with the intention of improving the quality of information provided by participants. Intensive training was provided over five days, which included background information regarding the study, ethics in research, expectations regarding behaviour and general conduct while in the field, processes for obtaining written informed consent, conducting an interview and completion of the questionnaire. The training manual is available from the authors on request. As most of the fieldworkers had no prior experience, ongoing support during the six-week data collection period was also provided. Debriefing sessions were held at the end of each day with their supervisor and weekly with the Project Manager and Project Coordinator. These sessions included discussions around challenges encountered, possible solutions for the challenges and the opportunity for fieldworkers to seek support in relation to distressing situations encountered during the interviews. Fieldworkers were advised on strategies to avoid confrontation with male partners of participants. The timing of questionnaire completion was adjusted to minimise the risk of encountering intoxicated partners of participants. In some instances, fieldworkers enlisted the support of trustworthy local male residents who could mediate when necessary. Supervisors were trained to monitor the emotional state of fieldworkers and identify any signs of stress. Referral pathways for counselling were identified, should referral be required.

Measurement - Questionnaire

The investigators developed the questionnaire, based on survey tools used previously in South Africa. The ten core questions of the Alcohol Use Disorders Identification Test (AUDIT) (Table 1) and the four CAGE questions (Table 2) were included in the questionnaire, as well as quantity estimates for alcohol consumption. In light of the sensitivity of the questions relating to alcohol consumption and reproductive health, additional sensitivity training was provided for fieldworkers by the Co–PI of the parent study. Each respondent was provided with an information pamphlet after recruitment, which contained information regarding levels of risky drinking, and local service providers offering assessment and counselling should they or anyone else in their social circle require such services. The pamphlets were also made available to the community as part of the awareness campaign.

Table 1: AUDIT questions

1. How often do you have a drink containing alcohol?
2. How many drinks containing alcohol do you have on a typical day when you are drinking? (Please note that one drink is equivalent to one can or bottle of beer, cider or coolers, one glass of wine, or one tot of spirits).
3. How often do you have six or more drinks on one occasion?
4. How often during the last year have you found that you were unable to stop drinking once you had started?
5. How often during the last year have you failed to do what was normally expected from you because of drinking?
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
7. How often during the last year have you had a feeling of guilt or remorse after drinking?
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
9. Have you or someone else been injured as a result of your drinking?
10. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down?

Table 2: CAGE questions

1. Have you ever felt you ought to cut down drinking?
2. Have people annoyed you for criticising your drinking?
3. Have you ever felt guilty about your drinking?
4. Have you ever had a drink first thing in the morning?

Data management

Data collection was managed by the South African Medical Research Council (MRC). Data were anonymised, with names and addresses stored separately from the questionnaires. Each questionnaire was allocated a study number. Data of interest were aggregated and analysed in a manner which ensured anonymity of all participants. Data stored electronically were filed in password protected locations.

Analysis

Descriptive statistics will be used to demonstrate demographic data and characteristics of participants relevant to their drinking habits and risk of Foetal Alcohol Spectrum Disorder (FASD), such as the availability of alcohol in their area of residence, race group, drinking patterns, religiosity, type of alcohol consumed, how alcohol is purchased, amount of disposable income available, food security, family history of alcohol use, smoking habits etc.

The analysis of the collected data will focus on identifying which currently validated brief AUDIT screening questionnaire/s correlate best with the overall score of the complete AUDIT questionnaire as the gold standard. An AUDIT score >=5 will be taken as an indication of hazardous or harmful drinking. This is lower than the conventional cut point, which is a total score of 8 applicable to men and women. The lower cut point was selected in response to recent research indicating that the cut point for women should be lowered, with 5 selected as the most appropriate cut point (Reinert & Allen, 2007). This analysis will be repeated with a cut off score >= 8 for the full AUDIT.

The brief AUDIT questionnaires to be used in the comparison are AUDIT-C, AUDIT-3, AUDIT-4, AUDIT-PC and AUDIT-QF. The questions for each test are

represented in Table 3.

Table 3: Questions comprising each Brief AUDIT screening questionnaire (Question number in the full AUDIT questionnaire indicated in brackets)

AUDIT-C
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
3. How often do you have six or more drinks on one occasion? **(Q3)**
AUDIT-3
1. How often do you have six or more drinks on one occasion? **(Q3)**
AUDIT-4
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
3. How often do you have six or more drinks on one occasion? **(Q3)**
4. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down? **(Q10)**
AUDIT-PC
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
3. How often during the last year have you found that you were not able to stop drinking once you had started? **(Q4)**
4. How often during the last year have you failed to do what was normally expected from you because of your drinking? **(Q5)**
5. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down? **(Q10)**
AUDIT-QF
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**

Receiver Operating Characteristic (ROC) plots, which plot the sensitivity vs 1-specifity of a test, are used to determine the ability of a test to identify correctly those who have a particular condition vs those who do not. The area under the curve (AUROC analysis) provides an indication of this ability. An area under the curve equal to 1 indicates a perfect test, whereas 0.5 indicates that the results of the test do not differ significantly from chance. Values from 0.9 - 1.0 indicate excellent, 0.8 – 0.9 good, 0.7 - 0.8 fair, 0.6 - 0.7 poor and 0.5 - 0.6 failed performance (Tape, n.d.).

AUROC analyses will be utilised in order to determine the test with the best accuracy, with the brief AUDIT compared to the full AUDIT score as the gold

standard. AUROC analysis will also be used to determine the optimal sensitivity vs specificity cut-off points to minimise misclassification. The analysis will include identification of the optimal cut off score for the different brief AUDIT questionnaires tested.

Additionally, analysis will be done to determine whether a single screening question can be used to identify a high likelihood of dependent drinking, as indicated by a full AUDIT score of 20 or more. This question could serve as the initial screening question. Should an individual be identified as a possible dependent drinker by the initial question, no further questions will be required. Individuals not identified as possible dependent drinkers by the initial question will be asked all remaining questions in the screening questionnaire.

The analysis will be done separately for rural and urban populations, as the sampling method was different for the two groups, in addition to demographic differences, such as different languages, cultures and socio-economic environments. A sensitivity analysis will also be performed excluding and including those women who report binge drinking, defined as five or more drinks on one occasion (Shield, et al., 2014).

Dissemination

Data collection was done in 2006 and findings were fed back to participants at that time. It is not intended to share the results of this study with study participants specifically, as many of them are likely to have moved away and the project is no longer active in the area.

The results of the study will be submitted in article format for consideration for publication in South African journals relevant to primary care services. The findings will be shared with primary care communities via local conferences.

The results will be disseminated to alcohol interest groups who may wish to use the information to influence policy.

Budget

Table 4: Budget requirements

STATA IC 15.0 license (six months student license)	R1174
Printing	R100
Postage	R400
Office costs (electricity, internet access, use of computer, etc.)	R200
Total budget:	**R1874**

Ethical considerations

Potential risks

Collecting data regarding women misusing alcohol was done sensitively, as social sanction and therefore stigma is attached to this lifestyle behaviour, particularly alcohol use during pregnancy. Fieldworkers were trained by the Co-PI of the original study to equip them with appropriate skills and attitudes to conduct interviews during the survey. Participants were advised that their responses would be treated confidentially, i.e. names would not be recorded on the questionnaires, names could not be easily matched to the questionnaires by someone who was not a member of the research team and their completed questionnaires would be stored in a locked filing cabinet.

Participants were provided with contact details of local resources for assistance with alcohol abuse, other drug abuse, reproductive health services and self-help groups for women.

Potential benefits of the proposed research to subjects and others

The envisaged benefits of the current research are unlikely to provide direct benefit to the participants. However, the information gained from this study will be used to make recommendations regarding screening of women of childbearing age for the risk of alcohol exposed pregnancy and alcohol related illness. The envisaged benefits will therefore assist in improving the opportunities to identify women at risk of an AEP and, in the long-term, is likely to improve health outcomes in the country in relation to the quadruple burden of disease. Ultimately, this could potentially result in a safer society with improved economic growth. Should these benefits be realised, all citizens within the country will enjoy the improvements resulting from the reduction of hazardous and harmful drinking of alcohol.

Importance of the knowledge to be gained

The knowledge gained as a result of this study will assist in reducing alcohol consumption among women of childbearing age who consume hazardous or harmful amounts of alcohol by providing means to identify such women, which can realistically be included in the routine delivery of primary care services.

As the risk posed to participants was minimal, the benefits related to the knowledge gained will outweigh the risks.

The resultant questionnaire will be communicated to the health community via submission of a research report to the Western Cape Government Health Department and the Gauteng Department of Health, and via publication in a peer-reviewed journal. It is intended that the screening tool be administered routinely for all women attending primary care facilities. As national guidelines and/or policy are the most effective way of ensuring nationwide implementation of best practice, it is hoped that the study findings will be included in such documents.

Recruitment and informed consent

A consent form was signed by each survey respondent prior to commencement of questioning, and after a full explanation of their rights had been provided in their language of choice. All householders invited to participate were free to decline. Illiterate participants were requested to sign the consent form by means of an "X". As an additional safeguard, an adult member of the community was requested to witness the reading of the consent form to the illiterate participant as part of the consent process.

Ethical and Regulatory Compliance

This protocol complies with the requirements of the Declaration of Helsinki (2013) and Ethics in Health Research: Principles, Structures and Processes (2015; DOH)

Ethics approval was granted for the initial research (UCT HREC Ref# 381/2005) (UP HREC Ref# 121/2005). Ethics approval will be sought for the current analysis.

Limitations

As data was collected only in women aged 18-44 years, the recommendation for the screening questionnaire can only be applied to women in this age group.

As with similar studies, the validity of self-reported alcohol measures may not be accurate. However, steps were taken to mitigate this risk, e.g. reassuring participants of the confidentiality of the information provided and the use of peers as interviewers, in part to improve the validity of the information provided.

Asking both the CAGE and AUDIT questionnaires during the same interview may have affected the answers provided for the second questionnaire.

Timeline

Data analysis will be completed within four weeks and write up concluded for in the following four weeks. The draft thesis will be submitted for review and revised in response to feedback.

Authorship

The author of the thesis is Dr G Labadarios.

[4855 words]

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Part B: A structured literature review

Background

The earliest archaeological evidence of a fermented beverage dates back to 7000 BC in the Yellow River Valley in China (Penn Museum, 2018). Since then, alcohol has become an integral part of life in almost all cultures. In ancient cultures, mythological pantheons in each continent included deities associated with alcohol. Dionysius, from the Greek pantheon, had the power to inspire and to create ecstasy (Encyclopaedia Brittanica, 2018). Perhaps this provides an indication of why alcohol has such a pervasive presence, as it is perceived to be a means of escaping the cares and woes of life. Or, in the words of a pregnant woman recently diagnosed with HIV, “it's better for me if I drink, at least the stress is going away” (Watt, et al., 2014). In many cultures, life’s milestones are celebrated with alcohol – births, graduations, marriages, retirement and family events.

Nevertheless, alcohol is associated with net health and social problems in almost all societies where it is consumed (Shield, et al., 2014).

The tale of these problems can be told in numbers – the number of victims of alcohol related crime, violence and accidents, deaths related to alcohol induced illnesses, babies with alcohol related birth defects, working days lost due to alcohol-related sick days and the amount of money lost to GDP (gross domestic product) due to alcohol-related impaired performance, as examples (Rehm, et al., 2003) (May, et al., 2007) (Matzopoulos, et al., 2014) (Shield, et al., 2014) (World Health Organisation, Management of Substance Abuse Unit, 2014) (Olivier, et al., 2016) (National Department of Health, 2016)

Health care professionals in primary care can contribute significantly to reducing these outcomes for individuals under their care who consume hazardous or harmful amounts of alcohol by screening for this behaviour and referring those identified to be at risk for brief motivational interviewing. Validated screening tools suitable for use in primary care are available to identify those who drink at hazardous and harmful levels (Reinert & Allen, 2007) (World Health Organisation, Management of Substance Abuse Unit, 2014). Referral for brief motivational interviewing and/or treatment has been shown to be effective in reducing alcohol consumption (World Health Organisation, 2002) (World Health Organisation, 2010).

This literature review will examine the current situation in relation to alcohol consumption and consequent harm to individuals and society, as well as current advice in relation to mitigation of these harms by means of screening and intervention in primary care health services, with a particular focus on women of reproductive age.

Objectives of the literature review

1. Describe the global and local health impact of excessive alcohol consumption
2. Describe existing screening tools which can be administered in primary care settings with minimal disruption to services, particularly in relation to time constraints
3. Identify screening tools and interventions validated for implementation in South African primary care settings

Methodology

PubMed and Google Scholar databases were searched for relevant literature. In PubMed, the MeSH headings “alcohol drinking” and “binge drinking” were used with selection of subheadings relevant to the topics of interest, i.e. “adverse effects”, “diagnosis”, “complications”, “economics”, “mortality”, “prevention and control”, “women” and “threshold”.

Additional articles were identified from the reference lists of retrieved articles.

Similar terms were used in Google Scholar, which was also used to retrieve specific articles of interest.

Articles selected considered the cut-off points to be used in screening tests to identify harmful and hazardous drinking particularly in women and the effectiveness of various screening tests to identify harmful and hazardous drinking, differentiated the results of findings by gender, explored issues around alcohol exposed pregnancies or alcohol related birth defects, considered alcohol related costs to society, or provided an evaluation of the effectiveness of intervention programmes.

The following exclusion criteria were applied:

1. Articles not published in English

2. Research performed solely on adolescents, men or women older than 44 years of age

3. Animal studies

Quality of the articles

The quality of the articles included in this review was assessed using guidelines from the Centre for Evidence Based Medicine at the University of Oxford. The majority of studies reporting on the validity of various screening tests to identify hazardous and harmful drinking did not blind assessors administering the tests. In most articles, the reference test and the comparator test were administered during the same interview.

Findings of the systematic reviews were adequately reported, but older reviews were not always clear regarding the search methods used to identify articles. It is therefore difficult to be certain that significant studies were not omitted from the review. One of the reviews reported very clearly on the quality of the articles reviewed, however the remainder made reference to the quality evaluation having been done, but did not report explicitly on the results of the evaluation.

However, the remaining criteria for quality were largely met in the majority of the articles.

Global context

The World Health Organisation's (WHO) Global Status Report on Alcohol and Health 2014 identifies the prevention and reduction of harmful alcohol use as a public health priority, noting it to be among the top five risk factors for disability, disease and death throughout the world (World Health Organisation, Management of Substance Abuse Unit, 2014).

Alcohol consumption in excess of recommended limits causes 3.3 million deaths per year, which represents 5.9% of all deaths globally. These estimates include the health benefits conferred by moderate alcohol consumption on ischaemic heart disease, ischaemic stroke and diabetes (World Health Organisation, Management of Substance Abuse Unit, 2014). However, benefits associated with moderate drinking are lost if the individual also engages in heavy episodic drinking (Parry, et al., 2011). More recently, some studies have raised the possibility that the protective effect observed with moderate alcohol consumption may be due to factors such as lifestyle choices and socio-demographic factors rather than alcohol consumption (Schütze, et al., 2013) (Bergmann, et al., 2017).

In 2012, 5.1% of disability-adjusted life years were attributable to alcohol consumption (World Health Organisation, Management of Substance Abuse Unit, 2014).

Alcohol results in substantial societal costs, including direct costs, i.e. costs relating to health care, the justice system and damage to property, indirect costs, i.e. the effect of alcohol consumption on economic output and productivity and intangible costs, e.g. pain, suffering and diminished quality of life. In 2009, these costs amounted to €125bn for the European Union, £21bn for the UK and US$233bn for the USA (World Health Organisation, Management of Substance Abuse Unit, 2014).

A study in Thailand calculated the direct and indirect costs attributable to alcohol in 2006 as US$9627m or 1.99% of GDP, with indirect costs contributing 96% of the total cost (Thavorncharoensap, et al., 2010).

South African context

The WHO Global Status Report on Alcohol and Health documented a consumption of 58.5g of alcohol per day among those who drink in South Africa, one of the highest levels in Africa. Among drinkers, 25.6% engage in heavy episodic drinking (60g[3] or more of pure alcohol consumed on one occasion in the 30 days prior to data collection). Alcohol attributable deaths from all causes constitute 6.4% of all deaths in South Africa, the second highest proportion for alcohol attributable deaths in Africa, surpassed only by Namibia at 6.9%. This represents 787 749 years of life lost. Furthermore, 6.2% of disability in South Africa is attributable to alcohol (World Health Organisation, Management of Substance Abuse Unit, 2014).

Alcohol-attributable economic costs in 2009 were estimated at 10-12% of GDP (Matzopoulos, et al., 2014). In the same year, health received 14% of the national budget which equated to R99.8bn (National Treasury, Republic of South Africa, 2010)

Alcohol has a multi-level impact on South Africa's well-documented quadruple burden of disease - as a necessary cause for diseases caused only by alcohol (Lund, et al., 2013), a contributory cause for the genesis of communicable (Bhana, et al., 2017) and non-communicable diseases (Parry, et al., 2011) (Shield, et al., 2014) and as an exacerbating factor for many of these diseases resulting in less favourable outcomes and increased mortality rates (Morojele, et al., 2016) (Bhana, et al., 2017). In relation to maternal and child health, South Africa has the highest rate of Foetal Alcohol Syndrome (FAS) in the world (May, et al., 2007) (Olivier, et al., 2013) (Olivier, et al., 2016).

[3] 8g alcohol = 1unit alcohol = 25ml of 40% spirits, 80ml of 12.5% wine or 200ml of 5% beer

Recommended actions

The WHO's Global Strategy to Reduce the Harmful use of Alcohol recommends 10 areas for incorporation in national programmes (Table 1).

Table 1: Key areas to address to reduce the harmful use of alcohol (World Health Organisation, 2010)

Area
1. Leadership, awareness and commitment
2. Health services' response
3. Community action
4. Drink-driving policies and countermeasures
5. Availability of alcohol
6. Marketing of alcoholic beverages
7. Pricing policies
8. Reducing the negative consequences of drinking and alcohol intoxication
9. Reducing the public health impact of illicit alcohol and informally produced alcohol
10. Monitoring and surveillance

In Area 2, Health Services' Response, it is recommended that screening and treatment programmes are provided in primary care settings, amongst other actions.

The Alcohol Use Disorders Identification Test (AUDIT) screening questionnaire was developed on the recommendation of the 1979 WHO Expert Committee for Problems Related to Alcohol (World Health Organisation, 1980). The 10 questions in the AUDIT questionnaire were selected from an original 150-item interview, tested on a total of 1888 patients in Australia, Bulgaria, Kenya, Mexico, Norway and the USA. Although designed for use in all cultures and genders in primary care services, validation prior to implementation in a particular setting is recommended, due to the influence of culture on drinking behaviours and the need to ensure that the questionnaire will accurately identify those at risk in the specific setting (Saunders, et al., 1993). Since that time, AUDIT has been validated in many countries, including different population groups in North America (Bradley, et al., 2003) (Frank, et al., 2008), South America (Lima, et al., 2005), Europe (Neumann, et al., 2004) (Foxcroft, et al., 2014), Asia (Kim, et al., 1999) and Africa (Adewuya, 2005).

Although accurate, it can take 2-4 minutes to administer, which is too long for routine implementation in primary care settings (de Meneses-Gaya, et al., 2009). For that reason, several brief versions of the full AUDIT, varying from one to four questions, summarised in Table 2 below, have been tested (Reinert & Allen, 2007) (de Meneses-Gaya, et al., 2009).

Table 2: AUDIT questions

Full AUDIT – 10 questions
1. How often do you have a drink containing alcohol?
2. How many drinks containing alcohol do you have on a typical day when you are drinking? (Please note that one drink is equivalent to one can or bottle of beer, cider or coolers, one glass of wine, or one tot of spirits).
3. How often do you have six or more drinks on one occasion?
4. How often during the last year have you found that you were unable to stop drinking once you had started?
5. How often during the last year have you failed to do what was normally expected from you because of drinking?
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
7. How often during the last year have you had a feeling of guilt or remorse after drinking?
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
9. Have you or someone else been injured as a result of your drinking?
10. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down?
ABBREVIATED VERSIONS OF THE AUDIT QUESTIONNAIRE **(Question number in the full AUDIT questionnaire indicated in brackets)**
AUDIT-C
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
3. How often do you have six or more drinks on one occasion? **(Q3)**
AUDIT-3
1. How often do you have six or more drinks on one occasion? **(Q3)**
AUDIT-4
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
3. How often do you have six or more drinks on one occasion? **(Q3)**
4. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down? **(Q10)**
AUDIT-PC
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
3. How often during the last year have you found that you were not able to stop drinking once you had started? **(Q4)**
4. How often during the last year have you failed to do what was normally expected from you because of your drinking? **(Q5)**
5. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down? **(Q10)**
AUDIT-QF
1. How often do you have a drink containing alcohol? **(Q1)**
2. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**

The full AUDIT questionnaire has yielded valid results for the questions in all settings, with adjustments in the cut off points recommended in several sites and occasional adjustments to the questions recommended both by gender and culture (Adewuya, 2005) (Reinert & Allen, 2007).

Several studies report resistance from interviewees in response to the questions regarding alcohol related problems (Adewuya, 2005), and one study identified reported on the effect of sequencing of the questions on the overall score. However, although sequencing revealed a statistically significant difference in the total score for questionnaires with different sequencing, the difference was not clinically significant (Bischof, et al., 2005).

In 2003, Bradley et al demonstrated that AUDIT-C, comprised of the first three questions of the full AUDIT questionnaire, performed as well as the full AUDIT in identifying hazardous and harmful drinking as compared to diagnostic interview (Bradley, et al., 2003). However, they recommended that AUDIT question 3, “How often do you have six or more drinks on one occasion?”, be adapted for the female population to ask “How often do you have four or more drinks on one occasion?”. The majority of studies since that time have repeated the findings of the Bradley study (Reinert & Allen, 2007) (Frank, et al., 2008) (de Meneses-Gaya, et al., 2009) (Kaarne, et al., 2010) (Johnson, et al., 2013) (Seth, et al., 2015).

In the USA and Russia, a screening tool consisting of a single question has been developed for the identification of binge drinking in women, which correctly identified 86% of women in the American study (n=286) and 99% of women in the Russian study (n=689) (Stewart, et al., 2010) (Balachova, et al., 2015).

However, the single question AUDIT-3 has been demonstrated to be unreliable in two studies in Southern Africa (Seth, et al., 2015) (Morojele, et al., 2016). In addition, the South African study found that AUDIT-PC provided the closest correlation with the full AUDIT score rather than AUDIT-C (Morojele, et al., 2016).

Studies repeatedly demonstrate differences in the ability of various screening tests to identify hazardous and harmful drinking behaviour by gender, as well as differences in the optimal cut off points for men and women (Bradley, et al., 2003) (Adewuya, 2005) (Lima, et al., 2005) (Reinert & Allen, 2007) (Frank, et al., 2008) (Bradley, et al., 2009) (Kaarne, et al., 2010) (Johnson, et al., 2013) (Foxcroft, et al., 2014) (Seth, et al., 2015) (Morojele, et al., 2016).

In addition to cultural and gender variations, the AUDIT questionnaire appears to perform differently in various age categories. It has consistently been shown to have reduced sensitivity among older adults. Studies of different populations have shown that when used for the screening of adolescents, it is advisable to adjust the cut off points to reflect accurately the potential harm resulting from a

particular level of alcohol consumption (Reinert & Allen, 2007) (de Meneses-Gaya, et al., 2009).

Gender effects

A given volume of alcohol will result in higher blood alcohol concentration in women than men, due to the lesser proportion of water for a given body weight in women. Absorption of alcohol is also accelerated in women relative to men. The smaller distribution volume in women results in delayed elimination of blood alcohol relative to men, resulting in a higher blood alcohol concentration for a longer duration for a given volume of alcohol consumed (Erol & Karpyak, 2015).

Alcohol is metabolised differently in men and women with absorption being quicker in women than men. It appears that hormonal levels affect the absorption, distribution and metabolism of alcohol, although the mechanisms of action are not clear. Oestradiol reduces neuronal damage related to alcohol withdrawal. (Erol & Karpyak, 2015).

Women are less likely to experience alcohol withdrawal symptoms, less likely to have seizures associated with alcohol withdrawal and less likely to experience delirium tremens than men (Erol & Karpyak, 2015).

Additionally, gender affects choices in relation to alcohol. In most cultures, social sanction in relation to alcohol usage is stronger for women than men, especially during pregnancy, which translates to lower prevalence of alcohol consumption, alcohol use disorders and alcohol related illness among women (World Health Organisation, Management of Substance Abuse Unit, 2014) (Erol & Karpyak, 2015). In recent years, national consumption figures demonstrate that this difference is decreasing over time (Erol & Karpyak, 2015). However, although prevalence of alcohol related illnesses is higher among men, women who drink will experience these illnesses after a shorter duration of alcohol use and at lower levels of alcohol consumption (Bradley, et al., 2003) (Erol & Karpyak, 2015). Additionally, women who drink die at a younger age due to natural diseases and/or alcohol related conditions (Erol & Karpyak, 2015). The increased susceptibility of women to the harmful effects of alcohol, as well as the possibility that a woman's drinking behaviour may affect her unborn children, therefore justify equal focus on the identification of hazardous and harmful drinking in women, despite the lower prevalence of harm.

Since the initial validation of AUDIT and determination of the cut off point for harmful and hazardous drinking, subsequent research has demonstrated that harm caused by alcohol consumption occurs at lower levels of consumption than initially believed (Reinert & Allen, 2007). It is therefore suggested that the most appropriate cut off point for the full AUDIT questionnaire in women is 5, reduced from the initial cut off point of 8 for both women and men. The current recommended cut off point for men is 6. Additional research to determine a

gender specific abbreviated version of the full AUDIT questionnaire has been recommended (Reinert & Allen, 2007).

In light of these cultural and physiological differences, and in response to recommendations, it is advisable to test screening tools separately for each gender, both to validate the questions used and to determine the optimal cut off point which will accurately reflect the level of alcohol consumption and drinking patterns at which harm is likely to occur, according to gender.

Alcohol-related cultural practices specific to South Africa

Since the 18th century, workers in South African agricultural communities in the Western Cape were given wine rations as part payment towards their wages. Although this practice was outlawed in 1961 and the ruling enforced from the early 2000s, the drinking culture engendered by this practice persists. This manifests in affected communities as a widespread acceptance of weekend drunkenness as a norm for men and women, including pregnant women. Additionally, drinking in such communities tends to be a group activity, valued as a means to unite the community, promote friendship and provide social support (Gossage, et al., 2014) (Watt, et al., 2014).

This cultural background combined with erroneous beliefs regarding alcohol in these communities and limited knowledge regarding its teratogenic effects, results in the continued use of alcohol during pregnancy, particularly among primigravidas (Morojele, et al., 2010). Heavy episodic drinking, as manifested in the weekend drinking to excess in these communities, is particularly damaging to embryogenesis and foetal development due to the high blood alcohol concentration resulting from this pattern of consumption (May & Gossage, 2011).

In addition to these cultural influences on drinking practices and Foetal Alcohol Syndrome (FAS) rates, demographic characteristics compound the risk of alcohol exposed pregnancies resulting in foetal alcohol spectrum disorder (FASD) (May, et al., 2007) (May & Gossage, 2011). Women in these areas tend to be smaller in stature, have lower BMI, smoke tobacco, suffer nutritional deficiencies and complete fewer years of education, all of which are associated with increased risk of FASD (May, et al., 2004) (May, et al., 2014) (Montag, 2016) (Olivier, et al., 2016) .

An additional challenge in preventing FASD is that high blood alcohol concentrations in the mother at any stage during the gestation, including at conception and the first few weeks of gestation prior to recognition of the pregnancy, can result in teratogenic effects. It is therefore preferable to intervene prior to conception to prevent an alcohol exposed pregnancy (Morojele, et al., 2010) (Balachova, et al., 2015).

Studies in Sweden and Canada indicate that FAS and FASD represent significant cost burdens to society, as a result of direct and indirect costs. Direct costs relate to the increased care requirements of individuals affected by FASD. Indirect costs relate to the loss of earnings by carers of children with FASD, loss of economic productivity from affected individuals, increased rates of antisocial behaviour, drug abuse and criminal activity among FASD sufferers, which may incur societal costs relating to foster care, court proceedings and incarceration, as well as costs relating to services required by those affected by the activities of the FASD sufferer (Popova, et al., 2014) (Ericson, et al., 2017). In South Africa, a study published in 2011 estimated the FAS/PFAS (partial foetal alcohol syndrome) attributable costs for paediatric healthcare in the Western Cape in 2009/2010 to be between US$ 53 and 71m (Credé, et al., 2011). A master's thesis estimated the costs in educator time attributable to FAS/PFAS in public primary schools in the Western Cape in 2012 to be US$ 7m for disruptions, US$ 5.8m for additional educational assistance and US$ 3.9m for learners repeating an academic year (Makin, 2017).

Intervention in SA

South Africa's National Development Plan 2030 acknowledges the magnitude of the problem presented by hazardous and harmful alcohol consumption, naming alcohol abuse as a priority area for intervention (National Planning Commission, 2012)

As reported above, the WHO recommends screening and brief motivational interviewing and/or treatment, which has been shown to be effective in reducing harmful and hazardous alcohol consumption (World Health Organisation, 2010) (World Health Organisation, 2018). However, South African studies do not demonstrate the same degree of benefit experienced in other countries (Peltzer, et al., 2013) (Rendall-Mkosi, et al., 2013) (De Vries, et al., 2015). Nevertheless, in women of childbearing age, identification of those at risk of hazardous and harmful alcohol consumption will provide an opportunity to discuss contraception, which can reduce the risk of alcohol exposed pregnancy (Rendall-Mkosi, et al., 2013).

Morojele et al found that once women of childbearing age are aware of the risk alcohol presents to their unborn children, they are more likely to moderate their alcohol consumption when pregnant (Morojele, et al., 2010). Unfortunately, for many women, this increased awareness of the teratogenic effects of alcohol is gained by means of health education provided by health care professionals during their first pregnancy. Screening will therefore provide an opportunity to provide this health education to women before their first pregnancy.

Studies conducted in South Africa have identified that individuals who engage in hazardous and harmful alcohol consumption may not realise that their

consumption levels and/or patterns pose a risk to their health, due to community norms in relation to drinking culture (Gossage, et al., 2014). They may therefore not self-identify as being in need of assistance.

The challenges listed above can be ameliorated by implementing a universal screening programme for the identification of women at risk of hazardous and harmful alcohol consumption in primary care settings. As with tobacco, patients may wish to avoid a lecture regarding their lifestyle choices, may not wish to be stigmatised or may fear being treated with less priority due to their choice to engage in behaviour that puts their health at risk. As has been the case with tobacco, introducing routine screening for alcohol consumption may make it a more familiar and therefore accepted part of the health landscape, making patients more willing to accept the perceived intrusion into their personal lives, more aware of the harm posed by alcohol and more willing to provide accurate information about their drinking habits. Habituation to such questions may reduce the social desirability bias which leads to under reporting of alcohol use (Lange, et al., 2014).

Due to the resource constraints in the primary care sector in South Africa, any proposed screening tool for the identification of hazardous and harmful drinking should require minimal time for administration and have a low false positive rate to avoid spending time performing full evaluations of alcohol consumption volumes and patterns for individuals erroneously identified as being at risk. The test should also have high sensitivity, to ensure that as many at risk individuals as possible are identified.

Access to healthcare in South Africa is a challenge for many, more so for those in rural communities, who are additionally at increased risk of hazardous and harmful drinking practices, as described above. The reach of screening programmes may be extended by employing remote means of delivery, including mobile phone applications, internet technologies and telephone contact. These methods of intervention have been implemented elsewhere in the world with reasonable levels of success (Wilton, et al., 2013) (Bhochhibhoya, et al., 2015). The techniques do not seem to be as effective as face to face contact with patients, but given the shortage of health care providers in South Africa, the overwhelming numbers of patients requiring care (Rispel, 2016), the geographical challenges presented to health care professionals, the scale of the problem of alcohol abuse in South Africa and the increased prevalence of hazardous and harmful alcohol consumption in some rural areas, this method of intervention may assist in augmenting the impact of a national programme to reduce alcohol consumption.

Conclusion

Several brief screening tools have been identified and validated both locally and internationally. However, no screening tools have been tested specifically for women of childbearing age in South Africa. The proposed study will

undertake to identify which brief AUDIT screening questionnaire will be most appropriate to identify hazardous and harmful drinking among women of childbearing age in South Africa.

[3896 words]

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Part C: Publication-ready Manuscript

Abstract

Background: Alcohol consumption in South Africa is a major contributing factor to the quadruple burden of disease. Additionally, South Africa has the highest rate of Foetal Alcohol Syndrome in the world. As effective interventions are available for hazardous and harmful drinking, screening for this behaviour in primary care can potentially contribute to improving health outcomes and reducing the cost to society. Existing validated screening questionnaires are available to identify those who drink at hazardous or harmful levels. However, no tools have been validated for women of childbearing age in South Africa. Any screening tools recommended for implementation should be as brief as possible with high sensitivity and specificity to justify the time spent on screening and minimise time spent on false positive results.

Objectives: To identify the most appropriate existing abbreviated version of the Alcohol Use Disorder Identification Test (AUDIT) questionnaire for South African women aged 18-44 and determine whether adjustments are required for urban/rural residence or patterns of consumption (binge drinking vs non-binge drinking). Additionally, to determine whether a single question can be used to identify possible dependent drinking.

Methods: An existing dataset was used for the analysis, collected by means of household surveys conducted in 2006 in rural areas of the Western Cape and urban areas in Gauteng, South Africa. The Western Cape sample was selected by stratified random sampling of farm workers and the Gauteng sample was selected by cluster random sampling. AUROC analysis was used to compare the abbreviated questionnaires (AUDIT-C, AUDIT-3, AUDIT-4, AUDIT-PC, AUDIT-QF), CAGE and single questions to results of the full AUDIT screening questionnaire as the gold standard. Data was stratified in relation to binge drinking and the analyses repeated to determine any effect of drinking patterns on the results.

Results: AUDIT-4 and AUDIT-PC were the best performing brief questionnaires in both rural and urban settings. AUDIT-4 had AUCs of 97.52% and 96.87% in Western Cape and Gauteng respectively. AUDIT-PC had scores of 97.52% and 93.98% in Western Cape and Gauteng respectively. Stratification by drinking pattern did not substantially influence the results. The single question method of identification of possible dependent drinking is not supported by the results of this study, with AUCs of <75%.

Conclusion: AUDIT-4 appears to be the best brief questionnaire for the identification of hazardous and harmful drinking among women aged 18-44 in South Africa, with no adjustments required for urban/rural settings or drinking patterns.

[397 words]

Introduction

Harmful and hazardous alcohol consumption in South Africa is a major public health concern (Jacobs & Steyn, 2013) which contributes both directly and indirectly to the well-documented quadruple burden of disease and carries substantial societal costs (Matzopoulos, et al., 2014). Sustained, excessive alcohol consumption has a multi-level impact on each aspect of this burden of disease - as a necessary cause for diseases caused only by alcohol such as alcohol use disorders or alcohol related birth defects, a contributory cause for the genesis of diseases such as diabetes and hypertension, and as an exacerbating factor for many of these diseases resulting in less favourable health outcomes (Rehm, et al., 2003) (Seedat, et al., 2009) (Rehm, et al., 2010) (Burnhams, et al., 2014) (Saban, et al., 2014) (Morojele, et al., 2016) (Bello, et al., 2017) (Bhana, et al., 2017)

Addressing this single factor therefore has the potential to impact significantly on health outcomes and life expectancy related to these national priority conditions. This is recognised in South Africa's National Development Plan 2030 entitled "Our future – make it work" (National Planning Commission, 2012) which identifies alcohol abuse as a priority area for intervention.

Screening all patients attending primary health care services to identify those who may benefit from referral for brief motivational interviewing is recommended by the World Health Organisation as part of their Global strategy to reduce the harmful use of alcohol (World Health Organisation, 2010).

The ten question Alcohol Use Disorders Identification Test (AUDIT) was developed by the WHO Collaborative Project on Identification and Treatment of Persons with Harmful Alcohol Consumption in response to a recommendation of a WHO expert committee in 1980 (World Health Organisation, 1980) (World Health Organisation, 2018).

Brief screening questionnaires

Although primary care is the ideal setting for implementation of national screening programmes to identify individuals at risk of hazardous and harmful drinking (Fiellin, et al., 2000) (Mash, et al., 2015) (World Health Organisation, 2018), the over-utilised and under-resourced health system in South Africa (Rispel, 2016) make it essential that any proposed screening test requires minimal time for administration, is easy to apply and has high sensitivity and specificity to avoid time wasted in full evaluation of individuals with false positive screening results.

Abbreviated versions of the AUDIT questionnaire have been identified to facilitate utilisation in busy, high pressure clinical care settings (Reinert & Allen, 2007). However, it is not clear whether the abbreviated questionnaires will be as accurate in South African health care settings as elsewhere, as South Africa has a high prevalence of binge drinking. Some studies have reported that existing screening questionnaires may not accurately identify individuals at risk as a result of this drinking pattern, as exposure to high blood alcohol

concentrations may be masked if the volume of alcohol consumed on one occasion is averaged over a number of days (Peltzer, et al., 2011).

Optimal brief AUDIT questionnaires for utilisation in HIV clinics in South Africa have been identified (Morojele, et al., 2016). This study reported differing performance of the various screening questionnaires by gender.

The CAGE questionnaire with just four questions (see Table 2) was developed in 1970 and validated for use in primary care to identify problem drinking (Mayfield & Hall, 1974) (Fiellin, et al., 2000). It has been used previously in South African studies (London, et al., 1988) (Peltzer, et al., 2011) (Rendall-Mkosi, et al., 2013) (McLoughlin, et al., 2013) (Gossage, et al., 2014) (Morojele, et al., 2016).

A study in the US reported that a single question from the Quick Drinking Screen, ("During the previous three months, how often did you have four or more drinks on one occasion?") successfully identified women at risk of hazardous and harmful drinking due to binge-drinking (>85% for current drinkers) (Stewart, et al., 2010). This study was replicated in Russia with similar results (99% success) (Balachova, et al., 2015). However, a previous study in South Africa repeated the analysis using AUDIT-3 (How often do you have six or more drinks on one occasion?), which showed that this single question screening questionnaire was not suitable for the South African population (Morojele, et al., 2016).

Gender and Age

A study evaluating worldwide performance of the AUDIT questionnaire suggested that it may be of benefit to identify a subset of AUDIT questions applicable specifically to women, as women appear to be more sensitive to the effects of alcohol than men (Reinert & Allen, 2007). This suggestion is supported by other studies demonstrating differences in metabolism result in higher blood concentrations of alcohol for longer duration in women than men for a given volume of alcohol. This results in more tissue damage for women in comparison to men, and therefore higher impact on health outcomes related to alcohol. Additionally, most cultures apply different social conventions to men and women regarding alcohol consumption, with consequent implications for patterns of behaviour in relation to alcohol. (Erol & Karpyak, 2015).

In their review of worldwide performance of the AUDIT questionnaire, Reinert et. al. further identify that screening criteria for adolescents and older adults may be different to those for adults (Reinert & Allen, 2007).

As an additional consideration, women in their reproductive years who consume alcohol at hazardous or harmful levels are at risk of having an alcohol exposed pregnancy and/or a child with Foetal Alcohol Spectrum Disorder (FASD). Agricultural regions of the Western Cape Province of South Africa report the highest rate of Foetal Alcohol Syndrome in the world (May, et al., 2007) (Olivier, et al., 2013) (May, et al., 2016). This is due in part to local drinking culture which entails large volumes of alcohol consumed over weekends in communal settings which offer social support and recreation (Watt, et al., 2014). This culture was fostered by the historic practice of part

payment with alcoholic beverages to farm labourers, known locally as the "Dop" system, "dop" being the Afrikaans word for tot (London, 1999). Although this practice was outlawed in the early 1960s and the laws have been actively enforced since the early 2000's, the drinking culture engendered by this practice persists, as do the consequences.

In order to address the gaps in the literature as outlined above, this study seeks to identify a brief, accurate screening questionnaire for use in women aged 18-44 years for utilisation in South African primary care establishments through the following objectives:

1. Compare existing brief AUDIT questionnaires and CAGE questions to the full AUDIT questionnaire as the gold standard to determine the most accurate brief screening questionnaire in identifying women at risk of hazardous and harmful drinking
2. Determine the effect of residence location (urban/rural) on the accuracy of different screening questionnaires
3. Determine the effect of binge drinking (defined as five or more drinks on one occasion for women) on the accuracy of screening questionnaires
4. Determine whether a single question can be used to identify individuals with a high likelihood of dependent drinking

Methods

An existing dataset collected in rural and urban areas of South Africa in 2006 was utilised for the analysis. This study therefore represents a secondary data analysis of an existing dataset. The rural area included Cederberg, Swartland and Bergriver municipalities in the Western Cape Province, with a combined population of around 160 000 at the time of the survey. The urban area included Mamelodi, Eersterus and Moot suburbs of the City of Tshwane municipality in Gauteng Province, with a combined population of around 340 000 at the time of the survey. In both provinces, data was collected by means of a household survey administered by trained interviewers.

Ethics approval for the initial study was granted by the Health Sciences Research Ethics Committees of the University of Pretoria (UP HREC Ref# 121/2005) and University of Cape Town (UCT HREC Ref# 381/2005). Ethics approval for the current analysis was granted by the Health sciences Research Ethics Committee of the University of Cape Town (UCT HREC Ref# 322/2018).

Previously published papers from this dataset include (Morojele, et al., 2010) (Ojo, et al., 2010) (Peer, et al., 2013) (Muhwava, et al., 2016) (Amanuel, et al., 2018).

Sampling

Sample size was calculated based on a power of 0.85, an estimated prevalence of 10% for risky drinking, completed primary education as a risk factor amongst risky drinkers of 40% and amongst non-risky drinkers of 58% (known example of a risk factor utilised for the power calculation), and a significance level of 0.1. This resulted in an estimated sample size of 750 in the urban area and 619 in the rural area. To ensure an adequate number of participants to achieve the required power, the sample size was adjusted upwards using the variance inflation factor (VIF) given by (1/1-ρ2) on the computed sample, where ρ2 is the squared multiple correlation of the covariate of interest to 790 for the urban population and 650 for the rural population.

The study population was the total population of women (pregnant and non-pregnant) aged 18-44 years within the geographical areas defined above, representing a total population of around 500 000. In the urban site, cluster random sampling was applied. Eighty-two census enumeration areas were selected, from each of which ten households were randomly selected, identified with the assistance of aerial photographs. One woman aged 18-44 years was randomly selected from each household and invited to participate in the survey.

In the rural site, stratified cluster random sampling was applied. For the first stratum, farms were selected within the relevant municipalities, proportional to the total number of farms in each municipality. Using this proportional approach, at total of 150 farms were randomly selected from a total population of 1450 farms in the three municipalities. This number represented oversampling to allow for uncontactable, ineligible and non-functional farms. For the second stratum, within each farm all women aged 18-44 years in every household were invited to participate in the survey. This sampling method was chosen as there are on average seven households per farm and the farms are separated by large geographical distances. No incentives to participation were offered. Pregnant and non-pregnant women were included, as the aim of the study is to identify appropriate screening to be implemented in advance of conception. Women who had never consumed alcohol or were not current drinkers were excluded from this analysis. Women who declined to participate were not included at their request.

Twelve female fieldworkers were recruited from communities local to the survey, with the intention of improving the quality of information provided by participants. Intensive training was provided over five days, which included background information regarding the study, ethics in research, expectations regarding behaviour and general conduct while in the field, processes for obtaining written informed consent, conducting an interview and completion of the questionnaire.

Measurement

The questionnaire used for the survey included all ten questions from the AUDIT questionnaire (Table 1) and the four questions of the CAGE questionnaire (Table 2). The AUDIT questionnaire is designed to be applicable across cultures and genders (Babor & Grant, 1989) (Saunders, et al., 1993), although the authors recommend validation in each setting prior to implementation. Questions 1-3 relate to alcohol consumption, questions 4-6 measure alcohol dependence symptoms and questions 7-10 determine alcohol-related problems. The response to each question is measured by a five point Likert scale. Responses are summed for an overall score ranging from 0-40. Scores are then categorised into low risk (0-7), alcohol use in excess of low-risk guidelines (8-15), hazardous or harmful drinking (16-19; likely to result in harm eventually) and high-risk (20 or more; definite harm with the likelihood of current alcohol dependence) (World Health Organization, 2001). The questions for the AUDIT screening test are asked with reference to the preceding 12 months.

Additional data were collected in relation to demographics, level of connectedness / social support structures, health perceptions, use of reproductive health services, pregnancy experiences and fertility norms, smoking patterns, cultural beliefs and practices related to substance use (in particular during pregnancy), and knowledge of the effects of alcohol on pregnancy / child development.

Table 1: Full AUDIT questionnaire

1. How often do you have a drink containing alcohol?
2. How many drinks containing alcohol do you have on a typical day when you are drinking? (Please note that one drink is equivalent to one can or bottle of beer, cider or coolers, one glass of wine, or one tot of spirits).
3. How often do you have six or more drinks on one occasion?
4. How often during the last year have you found that you were unable to stop drinking once you had started?
5. How often during the last year have you failed to do what was normally expected from you because of drinking?
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?
7. How often during the last year have you had a feeling of guilt or remorse after drinking?
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
9. Have you or someone else been injured as a result of your drinking?
10. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down?

Table 2: CAGE questions

1. Have you ever felt you ought to cut down drinking?
2. Have people annoyed you for criticising your drinking?
3. Have you ever felt guilty about your drinking?
4. Have you ever had a drink first thing in the morning?

Analysis

Demographic data and characteristics of participants relevant to their drinking habits and risk of FASD were described for comparison between the two populations.

The scores of brief AUDIT screening questionnaires and the CAGE questionnaire were compared to a full AUDIT score of five or more (indicative of hazardous or harmful drinking) to determine which of the brief questionnaires performed best in the accurate identification of those at risk, as indicated by the full AUDIT questionnaire (the gold standard). The analysis included determination of the optimal cut off point for the brief questionnaire in doing so. The selected full AUDIT cut off of 5 is lower than the originally identified cut off point of 8 or more, applicable to men and women (Saunders, et al., 1993). The lower cut point was selected in response to more recent research indicating that the cut point for women should be lowered, with 5 selected as the appropriate cut point (Reinert & Allen, 2007).

The brief AUDIT questionnaires to be used in the comparison are AUDIT-C, AUDIT-3, AUDIT-4, AUDIT-PC and AUDIT-QF. The questions for each questionnaire are listed in Table 3.

Table 3: Questions comprising each Brief AUDIT screening questionnaire
(Question number in the full AUDIT questionnaire indicated in brackets)

AUDIT-C
4. How often do you have a drink containing alcohol? **(Q1)**
5. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
6. How often do you have six or more drinks on one occasion? **(Q3)**
AUDIT-3
2. How often do you have six or more drinks on one occasion? **(Q3)**
AUDIT-4
5. How often do you have a drink containing alcohol? **(Q1)**
6. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
7. How often do you have six or more drinks on one occasion? **(Q3)**
8. Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down? **(Q10)**
AUDIT-PC
6. How often do you have a drink containing alcohol? **(Q1)**
7. How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**
8. How often during the last year have you found that you were not able to stop drinking once you had started? **(Q4)**

9.	How often during the last year have you failed to do what was normally expected from you because of your drinking? **(Q5)**
10.	Has a relative, friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down? **(Q10)**
AUDIT-QF	
3.	How often do you have a drink containing alcohol? **(Q1)**
4.	How many drinks containing alcohol do you have on a typical day when you are drinking? **(Q2)**

Receiver Operating Characteristic (ROC) plots, which plot the sensitivity vs 1-specifity of a test, are used to determine the ability of a test to identify correctly those who have a particular condition vs those who do not. The area under the curve provides an indication of this ability (AUROC analysis). An area under the curve (AUC) equal to 1 indicates a perfect test, whereas 0.5 indicates that the results of the test do not differ significantly from chance. Values from 0.9 - 1.0 indicate excellent, 0.8 – 0.9, good, 0.7 - 0.8 fair, 0,6 - 0.7 poor and 0.5 - 0.6 failed performance (Tape, n.d.).
AUROC analyses were utilised to determine the brief AUDIT questionnaire with the highest accuracy and performance, compared to the full AUDIT score as the gold standard. The analysis was also used to determine the optimal sensitivity vs specificity at all possible cut-off points to minimise misclassification.

Further analysis was done to determine whether a single screening question could be used to identify possible dependent drinking. If so, using this as the first question in the screening process could render the remaining questions obsolete, thereby reducing the time required for screening for some patients. The individual questions chosen to explore for this purpose were the three questions related to dependence symptoms in the full AUDIT questionnaire.

Analysis was conducted separately for rural and urban populations, as the sampling method was different for the two groups, in addition to demographic differences, such as different languages, cultures and socio-economic environments.

A sensitivity analysis was performed excluding and including those women who report binge drinking. To report comprehensively on this issue, the samples were stratified in three ways:

- Binge pattern 1 – taking more than six drinks on one occasion less than monthly (i.e. less frequently than once a month)
- Binge pattern 2 – taking more than six drinks on one occasion at least monthly
- Binge pattern 3 – taking more than five or six drinks on one occasion as their usual drinking pattern

Binge pattern 1 was included in the analysis as this drinking pattern, although less likely to cause harm to the woman, will put her progeny at risk of FASD (Balachova, et al., 2015) (Montag, 2016). Binge patterns 2 and 3 are recognised as hazardous drinking patterns for the drinker (Shield, et al., 2014) (World Health Organisation, Management of Substance Abuse Unit, 2014).

Results

Demographic characteristics

The study recruited 412 women in the Western Cape and 606 women in Gauteng. Risk factors associated with alcohol consumption and with Foetal Alcohol Spectrum Disorder (May & Gossage, 2011) (May, et al., 2016); drinking habits, drinking culture and access to alcohol are reported in Table 4.

Table 4: Demographic characteristics[4]

Characteristic	**Western Cape n=412**	**Gauteng n=606**
Age (years)		
Mean	31	30
Median	32	29
Mode	32	24
Number of years in formal education		
<1-3 years	15.09 (62)	2.97 (18)
4-7 years	44.28 (182)	4.78 (29)
8-10 years	32.85 (135)	20.29 (123)
11-12 years	7.06 (29)	57.1 (346)
Tertiary education	0.73(3)	14.52 (88)
Employment status		
Unemployed	19.9 (82)	57.92 (351)
Part time	35.44 (146)	14.36 (87)
Full time	44.17 (182)	25.41 (154)
Self-employed	0.49 (2)	1.98 (12)
Smoking status		
Non smoker	6.2 (25)	7.72 (45)
Up to 5cpd[5]	45.41 (183)	6.52 (38)
6-20cpd	16.38 (66)	3.78 (22)
>20cpd	1.49 (6)	0.17 (1)
Not Applicable	30.52 (123)	81.82 (477)
Importance of religious belief		
Utmost	56.2 (231)	41.23 (249)
Great	23. 11 (95)	39.24 (237)
Some	10.71 (44)	14.24 (86)
Little	8.76 (36)	4.30 (26)
None	1.22 (5)	0.99 (6)

[4] *All results are represented as percentages with the corresponding numbers of participants indicated in brackets, with the exception of age which is shown only as numbers of participants*
[5] cpd = cigarettes per day

Marital status		
Legally married	29.85 (123)	20.13 (122)
Traditionally married	0.97 (4)	10.4 (63)
Cohabiting	34.71 (143)	5.94 (36)
Never married	30.34 (125)	58.58 (355)
Divorced / Widowed / Separated	4.13 (17)	4.79 (29)
Domestic violence		
Yes	34.71 (143)	19.47 (118)
No	45.87 (189)	52.81 (320)
Missing	19.42 (80)	27.72 (168)
Number of births		
0	12.14 (50)	23.6 (143)
1	27.67 (114)	26.73 (162)
2	26.94 (111)	22.94 (139)
3	19.42 (80)	15.18 (92)
4	8.25 (34)	6.93 (42)
More than 4	3.64 (15)	4.13 (25)
Is the foetus affected by alcohol		
Yes	78.64 (324)	82.01 (497)
No	12.86 (53)	3.63 (22)
Sometimes	2.18 (9)	1.49 (9)
Don't know	5.83 (24)	6.93 (42)
How often did you drink in your last pregnancy after confirmation of pregnancy		
Never	16.02 (66)	5.61 (34)
Monthly or less	8.74 (36)	1.32 (8)
2-4 x/month	5.34 (22)	0.66 (4)
2-3 x/week	4.61 (19)	0.5 (3)
4 or more x/wk	0.49 (2)	0.17 (1)
N/A (teetotal/nulliparous)	38.11 (157)	23.6(143)
Missing	26.7(110)	68.15 (413)
Likelihood of abstinence in next pregnancy		
Likely	29.13 (120)	6.44 (39)
Neither likely nor unlikely	0.73 (3)	0.50 (3)
Unlikely	4.85 (20)	0.66 (4)
Missing	65.29 (269)	92.41 (560)
How often do people in your household go hungry or have no food to eat		
Never	82.28 (339)	71.29 (432)
Seldom	5.35 (22)	3.96 (24)
Sometimes	7.79 (32)	22.44 (136)
Often	4.38(18)	1.98 (12)
Easy to buy alcohol in the community		
Strongly agree	20.54 (84)	72.4 (438)
Moderately agree	11.00 (45)	9.92 (60)
Neither agree nor disagree	1.22 (5)	4.79 (29)
Moderately disagree	20.29 (83)	3.97 (24)
Strongly disagree	46.94 (192)	8.93 (54)
Have you ever drank alcohol		
Yes	72.33 (298)	40.33 (244)
No	27.67 (114)	59.67 (361)
How often do you drink alcohol		
Never	52.43 (216)	71.95 (436)
Monthly or less	19.17 (79)	16.17 (98)
2-4 times per month	17.72 (73)	7.76 (47)
2-3 times per week	9.47 (39)	3.14 (19)
4 or more times per week	1.21 (5)	0.99 (6)
Where is alcohol bought		
I do not buy it	24.27 (100)	5.28 (32)
Liquor store	42.23 (174)	17.49 (106)
Supermarket / café	4.13 (17)	6.27 (38)
Spaza shop	1.94 (8)	5.28 (32)
Night club / disco	3.88 (16)	6.6 (40)
Shebeen	12.38 (51)	4.62 (28)
Restaurant/pub	10.92 (45)	10.23 (62)
Don't drink / Missing	52.18 (215)	74.59 (452)
When you are not paying for your alcohol, how do you get it		
I make it myself	2.18 (9)	1.65 (10)
I get it on credit	5.58 (23)	0 (0)
I work for it	14.81 (61)	1.98 (12)

I exchange goods for it	0.73 (3)	0.17 (1)
It is bought for me/ given to me	35.68 (147)	19.8 (120)
I take it without paying	7.77 (32)	0.5 (3)
Other	1.94 (8)	1.82 (11)
Don't drink / Missing	51.94 (214)	74.42 (452)
Type of alcohol typically consumed		
Beer	42.48 (175)	5.45 (33)
Cider	14.32 (59)	17.82 (108)
Bottled wine	9.22 (38)	10.40 (63)
Papsak	20.15 (83)	1.16 (7)
Coolers group	15.29 (63)	13.86 (84)
Spirits	11.89 (49)	4.46 (27)
Liqueur	10.92 (45)	9.74 (59)
Home brew	4.85 (20)	1.32 (8)
Don't drink / Missing	51.94 (214)	74.26 (450)
Where do you drink		
Home	41.75 (172)	18.15 (110)
Park / outdoors	15.53 (64)	7.76 (47)
Restaurants	1.21 (5)	12.38 (75)
Taverns	NA	4.46 (27)
Shebeen	7.77 (32)	2.15 (13)
Bar	2.91 (12)	4.95 (30)
Car park	2.18 (9)	1.16 (7)
Friend's home	35.19 (145)	18.98 (115)
Party	29.13 (120)	20.79 (126)
Festival / concert	7.77 (32)	10.40 (63)
Other	0.49 (2)	0.99 (6)
Don't drink / Missing	51.94 (214)	74.26 (450)
Drinking partner		
Alone	3.4 (14)	0.17 (1)
With friends	30.1 (124)	16.67 (101)
With relatives	1.7 (7)	4.95 (30)
With partner	12.14 (50)	5.94 (36)
With other	0.49 (2)	0.17 (1)
With whoever is in the place	0.24 (1)	(no data)
Don't drink / Missing	51.94 (214)	72.11 (437)
Family member with alcohol problem		
Mother	26.46 (109)	7.1 (43)
Father	36.41 (150)	11.72 (71)
Uncle	33.5 (138)	19.64 (119)
Aunt	29.13 (120)	9.41 (57)
Sister	22.09 (91)	7.43 (45)
Brother	27.18 (112)	17.00 (103)
Missing	0.48–1.21 (2-5)	3.80-4.79 (23-29)
In the past 30 days, how much of the time have you felt down-hearted		
All	3.16 (13)	2.97 (18)
Most	7.06 (29)	10.07 (61)
A good bit	6.08 (25)	8.42 (51)
Some	20.19 (83)	30.36 (184)
A little	32.6 (134)	24.92 (151)
None	30.9 (127)	22.61 (137)
In the past 30 days, how much of the time have you felt so low that nothing could cheer you up		
All	1.7 (7)	3.30(20)
Most	5.58 (23)	7.59 (46)
A good bit	2.43 (10)	6.27 (38)
Some	11.17 (46)	22.11 (134)
A little	20.87 (86)	26.57 (161)
None	58.25 (240)	33.99 (206)

Table 5: Partner drinking habits

How often does current partner have six or more drinks on one occasion		
Never	32.04 (132)	37.95 (230)
Less than monthly	6.55 (27)	6.27 (38)
Monthly	15.05 (62)	14.69 (89)
Weekly	25.00 (103)	9.08 (55)
Daily or almost daily	0.49 (2)	3.80 (23)
Missing	20.87 (86)	28.22 (171)
How many drinks does your partner have on any typical day when he is drinking		
None	25.97 (107)	31.85 (193)
1 or 2	6.80 (28)	7.59 (46)
3 or 4	10.44 (43)	14.36 (87)
5 or 6	11.65 (48)	9.90 (60)
7 to 9	8.50 (35)	2.81 (17)
10 or more	16.02 (66)	4.46 (27)
Missing	20.63 (85)	29.04 (176)

AUDIT and CAGE questionnaires were not completed for women who reported never having consumed alcohol (114 women (27.67%) in the Western Cape and 361 women (59.57%) in Gauteng) or for those who were not current drinkers at the time of the survey (111 women (24.94%) in the Western Cape and 83 women (13.7%) in Gauteng). This left 187 observations for analysis in the Western Cape and 162 in Gauteng.

Among the women who drank, 155 women in the Western Cape (37.62% of the total population, 52.01% of drinkers) and 72 women in Gauteng (11.88% of the total population, 45.86% of drinkers) had full AUDIT scores of 5 or above. The AUDIT scores and drinking patterns for each location are reported in Table 6.

Table 6: Total AUDIT scores and drinking patterns

	Western Cape n=189 (%)	**Gauteng n=237 (%)**
AUDIT score 0-4	26 (13.76)	81 (13.37)
AUDIT score 5-15	104 (55.03)	65 (10.73)
AUDIT score 16-19	25 (13.23)	5 (8.25)
AUDIT score 20-40	34 (17.99)	2 (3.30)
Infrequent binge drinking *(five or more drinks less than monthly)*	49 (25.92)	30 (4.95)
Frequent binge drinking *(five or more drinks at least monthly)*	107 (56.61)	54 (8.91)

Cronbach alpha scores for the responses to all ten AUDIT questions was 0.81 for the Western Cape and 0.79 for Gauteng. Cronbach alpha scores were lower for the brief AUDIT questionnaires due to the relatively low number of variables included (3 to 5). The Cronbach alpha scores in the Western Cape and Gauteng Provinces respectively for AUDIT-C, AUDIT-4 and AUDIT-PC were 0.66 and 0.63; 0.63 and 0.64; and 0.57 and 0.6. AUDIT-3 and AUDIT-QF were not suitable for this analysis as they include only one and two variables, respectively. The Cronbach alpha scores for the brief AUDIT questionnaires in the stratified data sets were all <0.6.

Testing of brief AUDIT questionnaires against the full AUDIT questionnaire – all participants

The first objective was to determine which of the brief AUDIT questionnaires provided the best correlation with a full AUDIT score of 5 and above. AUCs for all brief AUDIT scores were in excess of 90%, with the exception of AUDIT-3 in Gauteng and AUDIT-QF in both sites (See Table 7). AUDIT-PC and AUDIT-4 were the best performing questionnaires in both provinces, with AUCs in excess of 95%. Optimal cut off scores for the tests were similar with both provinces having an optimal cut off score of 4 for AUDIT-4. AUDIT-PC had an optimal cut off score of 4 in the Western Cape and 3 in Gauteng. At a cut off score of 3 in the Western Cape, the sensitivity of AUDIT-PC is 99.39% the specificity is 46.15% and the percentage correctly classified is 92.06. At a cut off score of 4 in Gauteng, the sensitivity of AUDIT-PC is 73.68%, the specificity is 98.77% and the percentage correctly classified is 86.62.

The results of the analyses for both sites are summarised in Table 7.

Table 7: Brief AUDIT results per province AUDIT score >=5 (Western Cape = rural; Gauteng = urban)

Brief AUDIT questionnaire	Location	AUC [CI]	Optimal cut off score	Sensitivity	Specificity	Correctly classified	PPV	NPV
AUDIT-C	Western Cape	94.96 [92.05- 97.87]	3	98.77	46.15	91.53	92.00	85.71
	Gauteng	92.76 [88.75 – 96.76]	4	84.21	88.89	86.62	87.67	85.71
AUDIT-PC	Western Cape	97.11 [95.06 – 99.15]	4	94.48	88.46	93.65	98.09	71.88
	Gauteng	95.12 [92.1 – 98.14]	3	90.79	86.42	88.54	86.25	90.91
AUDIT-4	Western Cape	97.50 [95.65 – 99.34]	4	98.77	73.08	95.24	95.83	90.48
	Gauteng	95.46 [92.49 – 98.43]	4	88.16	88.89	88.54	88.16	88.89
AUDIT-3	Western Cape	90.88 [86.86 – 94.91]	1	88.96	80.77	87.83	96.67	53.85
	Gauteng	85.22 [79.5 – 90.94]	2	63.16	92.59	78.34	76.19	83.56
AUDIT-QF	Western Cape	89.59 [84.31 – 94.87]	3	96.93	50.00	90.48	92.40	72.22
	Gauteng	88.67 [83.6 – 93.74]	3	78.95	87.65	83.44	85.71	81.61
CAGE	Western Cape	85.29 [77.96 – 92.61]	1	97.55	38.46	89.42	90.86	71.43
	Gauteng	71.69 [64.27 – 79.12]	1	68.42	71.60	70.06	69.33	70.73

Influence of drinking pattern on performance of brief AUDIT scores vs full AUDIT score

A second objective of the study was to determine whether a high prevalence of binge drinking in a community influences the ability of the screening test to identify those at risk of harm due to alcohol consumption.

In both locations, the results for comparison of the brief AUDIT scores with the full AUDIT score for each stratum mirrored the findings for the full data set in that AUDIT

4 and AUDIT PC outperformed the other brief versions of the questionnaires. The majority of AUCs for these two tests were above 90, with optimal cut off scores higher than those identified for the full data set. The results are summarised in Table 8.

Table 8: Brief AUDIT results per province, stratified for drinking pattern.

Brief AUDIT questionnaire	Location	AUC Binge 1[6] [CI]	AUC Binge 2	AUC Binge 3
AUDIT-C	Western Cape	94.69 [91.28 – 98.11]	Omitted[7]	Omitted[7]
	Gauteng	93.98 [89.53 – 98.43]	95.49 [90.76 – 1]]	94.23[87.4 - 1]
AUDIT-PC	Western Cape	97.79 [95.95 – 99.64]	Omitted[7]	Omitted[7]
	Gauteng	93.98 [89.63 – 98.34]	96.53 [92.91 – 1]]	91.03 [84.93 – 97.13]
AUDIT-4	Western Cape	97.52 [95.53 – 99.51]	Omitted[7]	Omitted[7]
	Gauteng	96.87 [94.39 – 99.36]	97.22[94.08 – 1]	94.87 [88.63 - 1]
AUDIT-3	Western Cape	Omitted[8]	Omitted[8]	Omitted[7]
	Gauteng	Omitted[8]	Omitted[8]	90.38 [80.48 - 1]
AUDIT-QF	Western Cape	90.69 [85.54 – 95.84]	Omitted[7]	Omitted[7]
	Gauteng	87.93 [81.05- 94.81]	92.36 [85.87 – 98.85]	84.62 [77.28 – 91.95]
CAGE	Western Cape	79.79 [60.59 – 98.99]	Omitted[7]	Omitted[7]
	Gauteng	63.98 [50.17 – 77.8]	52.08 [26.34 – 77.83]	79.49 [71.67 – 87.31]

[6] *Stratification for Binge categories 1 (more than six drinks on one occasion less than monthly) and 2 (more than six drinks on one occasion at least monthly) determined by AUDIT question 3 (How often do you have six or more drinks on one occasion?), binge category 3 (more than five drinks on one occasion when drinking) determined by AUDIT question 2 (How many drinks containing alcohol do you have on a typical day when you are drinking?).*
[7] All participants in this stratum had a full AUDIT score >5
[8] Stratification done on this question

Single question screening test

The third objective was to determine if a single question could be used to identify individuals with a high likelihood of dependent drinking, as indicated by an AUDIT score of 20 or above.

Each of the questions eliciting information regarding dependence symptoms in the AUDIT questionnaire (questions 4-6) were tested individually against a full AUDIT score of 20 or above to determine the ability of each single question to identify those with possible dependent drinking. For each of the questions analysed, AUCs were less than 75%. The single analysis with an AUC of 96% (i.e. for question 6 in Gauteng) had a sensitivity of 0.

The results of the analysis are summarised in Table 9.

Table 9: Single question for identification of possible dependent drinking

AUDIT question	Location	AUC	Optimal cut off score	Sensitivity	Specificity	Correctly classified	PPV	NPV
Q 4	Western Cape	72.27 [61.92 – 82.61]	0.569	32.35	97.42	85.71	73.33	86.78
	Gauteng	70.81 [14.2 - 1]	0.257	50	99.35	98.73	No +ves identified	98.73
Q 5	Western Cape	73.75 [63.68 – 83.82]	0.65	35.29	96.77	85.71	70.59	87.21
	Gauteng	73.23 [20.74 - 1]	0.629	50	100	99.36	100	99.36
Q 6	Western Cape	73.73 [63.98 – 83.48]	0.61	35.29	96.77	85.71	70.59	87.21
	Gauteng	96.13 [92.01 - 1]	0.292	0	100	98.73	No +ves identified	98.73

Discussion

As far as we are aware, this is the first study to examine specific questions in relation to the accuracy of brief alcohol screening questionnaires in women of childbearing age and the effect of binge drinking and locality on the accuracy of existing screening questionnaires for the South African population. The analysis indicated that brief AUDIT questionnaires outperform CAGE in the identification of problem drinking. It was not possible to detect a single screening question which could be used for the reliable identification of possible dependence. Stratification by location and binge drinking did not alter the findings substantially.

The results confirm the findings of previous studies relating to the higher prevalence of hazardous and harmful alcohol drinking in rural areas and the binge drinking pattern in rural areas (Olivier, et al., 2013) (May, et al., 2016). Binge drinking is associated with increased harm compared to non-binge drinking, in relation to both the woman's health and that of the foetus in cases where women continue to consume alcohol during pregnancy (May & Gossage, 2011) (World Health Organisation, Management of Substance Abuse Unit, 2014) (Balachova, et al., 2015).

This study is consistent with the findings of the Morojele et al study (Morojele, et al., 2016) to identify a brief screening questionnaire for HIV patients, in that the AUDIT-PC and AUDIT-4 are the best performing brief screening questionnaires in the South African setting. In the previous Morojele study, AUDIT-PC was the best performing test for the women in the sample, whereas for the current study, AUDIT-4 was the best performing test. In both studies, the differences in accuracy and performance between the two tests were marginal.

The stratification of the sample according to binge drinking did not alter the ranking of the brief screening questionnaires in relation to accuracy. The results for all three methods of stratification revealed that the tests performed the same in each stratum as in the full sample, where the sample allowed for meaningful analysis. This suggests that there is no benefit in using different screening tests in populations in South Africa known to have a high prevalence of binge drinking. The optimal cut off scores for the screening tests in the stratified data tended to be higher than for the full sample, suggesting that no alteration to the recommended cut off scores is necessary in populations with a high prevalence of binge drinking.

The appropriate cut off score for South African women of child bearing age for AUDIT-4, the best performing brief questionnaire, would seem to be 4 from the findings of the current study. AUDIT-PC was the second best performing test in this study. In this test, there was a discrepancy between the optimal cut off score for the rural and urban settings. The optimal cut off score for the Western Cape (rural setting) was 4, whereas in Gauteng (urban setting) it was 3. This is perhaps due to the two questions relating to dependence symptoms which are included in AUDIT-PC but not in AUDIT-4, with a very low prevalence of dependence amongst the population in Gauteng relative to that in the Western Cape. Comparison of the sensitivity, specificity, PPV and NPV at optimal cut off scores for each setting suggests that a cut off score of 4 would provide optimal accuracy and performance for application in both settings.

These findings, i.e. that AUDIT-4 and AUDIT-PC are the best performing brief AUDIT questionnaires in the South African setting, are very similar to, but not exactly the same as, the findings for patients in HIV clinics (Morojele, et al., 2016). In order to simplify the process of implementation of an additional national screening programme in primary care, it may be beneficial to choose a single brief screening questionnaire for

implementation across all primary care settings. A briefer test (AUDIT-4 consists of four questions whereas AUDIT-PC has five) may be beneficial in relation to time constraints. However, it would be perhaps be advisable to conduct further studies to confirm the optimal test for all relevant populations.

The attempt to determine a single question which accurately identifies women with possible dependent drinking was unsuccessful. The identification of such a question, to be asked as the initial screening question, has the potential to reduce the time impact of administration of the screening questions, as subsequent questions will not be necessary. This could be particularly beneficial in areas of high prevalence of harmful alcohol consumption, which are arguably the areas most likely to benefit from implementation of screening. Although these questions performed reasonably well in relation to AUCs, the sacrifice of sensitivity in comparison to the brief AUDIT questionnaires cannot be justified. To illustrate, for every 100 women screened in an area with a prevalence of dependent drinking of 8%, use of a single question with a sensitivity 32.35%, would identify only 2 or 3 (2.5) of the women.

Limitations

This study was done utilising an already existing dataset on which secondary analysis was done. However, some of the original researchers participated in this analysis and were available for consultation regarding discrepancies observed in the data. In the original study, data collection was done on one occasion only and both the CAGE and AUDIT questionnaires were administered during the contact, which may potentially have affected the answers provided for whichever questionnaire was administered last.

This study compared screening tests to another screening test, rather than with a definitive diagnosis. The abbreviated AUDIT questionnaires and single questions all included the same questions as the gold standard employed, i.e. the full AUDIT questionnaire. This will inevitably have inflated the correlation between the tests being compared. However, as the purpose of the study was to identify a brief, accurate screening test which performs as well as possible in relation to existing screening tests, the results answer the question posed. Future studies may wish to compare the performance of the abbreviated screening tests with a diagnostic test, such as full clinical evaluation using DSM criteria for alcohol use disorders.

As with similar studies of this nature, the self-reported alcohol consumption levels may not be accurate. However, steps were taken to improve the validity of this information, by using interviewers who were known to participants and assuring the participants of confidentiality.

Conclusion

The results of this study suggest that AUDIT-4 with a cut off score of 4 can be recommended as an appropriate screening tool to identify hazardous and harmful alcohol consumption among women aged 18-44 in South African primary care settings. There is no single question that can be substituted for AUDIT-4 or the full AUDIT questionnaire.

Larger studies to confirm these findings would be advisable prior to implementation of a national screening programme. In view of the similar findings of the studies done to date, it may be advisable to identify a single screening test which would perform satisfactorily across all primary care settings.

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[4911 words]

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Part D: Appendices

Appendix 1 – Ethics approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

16 May 2018

HREC REF: 322/2018

Prof L London
Public Health & Family Medicine
Falmouth Building

Dear Prof London

PROJECT TITLE: DETERMINATION OF A BRIEF AUDIT SCREENING QUESTIONNAIRE TO IDENTIFY WOMEN AT RISK OF HARMFUL AND HAZARDOUS ALCOHOL CONSUMPTION IN PRIMARY CARE SETTINGS (MMed-candidate-Dr G Labadarios) Sub-study linked to 381/2005

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 May 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

The HREC acknowledge that the student, Dr Grace Labadarios will also be involved in this study.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 322/2018

Appendix2: Acknowledgements

Author contributions

GL designed the study, did the primary analysis and wrote the different versions of the paper.

Acknowledgements to supervisors

NM oversaw the design of the study, the conduct of the analysis, commented on various drafts and interpretation of the data and approved the final manuscript. LL contributed to the design of the study, commented on various drafts and interpretation of the data and approved the final manuscript.

Appendix 3: SAMJ Instructions to Authors

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.

- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.